Case Report

A case of systemic lupus erythematosis with secondary APLA in a male

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease in which organs and cells undergo damage initially mediated by tissue-binding autoantibodies and immune complexes. Ninety percent of patients are women of childbearing years; people of all genders, ages, and ethnic groups are susceptible. Here is the case of 51 years male diagnosed with SLE with secondary antiphospholipid syndrome (antiphospholipid antibodie) and lupus nephritis confirmed by renal biopsy. The patient presented with vasculitic rash with proteinuria. Laboratory evaluation showed antinuclear antibody by immunofluorescence 3+, elevated activated partial thromboplastin time anti-cardiolipin antibody immunoglobulin G and lupus anticoagulant with dilute Russell viper venom time were positive. Renal biopsy showed International Society of Nephrology/Renal Pathology Society classification class III (A)+V nephritis. He was managed with low-dose glucocorticoid, oral vitamin K antagonist, and mycophenolate mofetil. The patient had a good clinical response.

Key words: Antiphospholipid syndrome, Dilute Russell viper venom time, Lupus nephritis, Systemic lupus nephritis

Systemic lupus erythematosis (SLE) results from interaction between genes or epigenetics and environmental factors, leading to abnormal immune responses that generate pathogenic autoantibodies and immune complexes that deposit in tissue, activate complement, induce cytokine and chemokine release causing inflammation, and over time lead to irreversible organ damage [1]. SLE is less common in males as compared to females, with a female-to-male ratio of about 9:1. However, males who do develop lupus tend to have more severe disease, including renal involvement, neuropsychiatric manifestations, and higher rates of thrombotic events when antiphospholipid antibodies (APLA) are present [2]. SLE is a multi-genic disease that includes homozygous deficiencies of early components of complement (C1q,r,s; C2; C4) and a mutation in TREX1 (encoding a DNAase) on the X chromosome [3]. Female sex is permissive for SLE with evidence for hormone effects, genes on the X chromosome, and epigenetic differences between genders playing a role. A gene effect in the promoter for interferon regulatory factor 5 that increases interferon (IFN) production is associated with SLE in all ancestries. MYH9/APOL1 associating with end-stage renal disease, hypomethylation of DNA-encoding genes, promoter regions, and/or transcription factors in CD4+ T cells, B cells, and monocytes. Environmental factors that stimulate SLE include ultraviolet light, smoking, crystalline silica, and Epstein-Barr virus infection [4]. The diagnosis of SLE is based on characteristic clinical features and autoantibodies. Two classification systems are currently in use: The 2012 Systemic Lupus International Collaborating Clinics criteria and the 2019 European League against Rheumatism/American College of Rheumatology (EULAR/ACR) classification in which clinical manifestations are weighted [5]. For EULAR/ACR criteria, a subject must have a positive antinuclear antibody (ANA) (≥1:80 by immunofluorescence) and a score of 10 (specificity 97%, sensitivity 93%).

In this case report, we are discussing an interesting case of SLE with secondary APLA and lupus nephritis in a middle-aged male. As SLE is relatively common in females, this article presents a male patient with typical rashes, renal involvement, and APLA positive.

CASE REPORT

A 51-year-male from Guntakal, Andhra Pradesh, a carpenter by occupation, presented to our emergency department with rashes on palms, soles, thigh, and elbows for the past 4 months. One month before admission to our hospital, he had a fall following which he sustained an injury over the left leg which progressed to cellulitis. He was admitted in an outside hospital and treated for cellulitis with intravenous (IV) antibiotics. His laboratory reports showed pancytopenia with deranged liver function (LFT) and

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renal function tests. Also found to have hypothyroidism, hence started on thyroxine 50 mcg. The patient has a personal history of alcohol intake for more than 20 years.

On general physical examination, the patient was pallor, and maculopapular rashes were noted over the palms, around both elbows, left thigh, and soles (Fig. 1). Dystrophic nails were there. Peripheral pulses were felt equal in all limbs. Vitals showed blood pressure of 110/70, heart rate of 78/min, respiratory rate of 14/min, and SpO_2 97% on room air. Musculoskeletal system examination was normal and no joint swelling or restricted mobility was noted. Other system examinations were also unremarkable.

Laboratory work-up revealed hemoglobin of 7 g%, total white blood cell count of 2500/mm^3, platelet count of 1.01 lakh/mm^3, and peripheral blood smear showed dimorphic anemia with leukopenia. Lactate dehydrogenase was 300, reticulocyte count was 1.8, and Direct Coomb's test was negative which implies no significant hemolysis. LFT showed mildly deranged liver enzymes with aspartate aminotransferase of 90, alanine aminotransferase of 33, and gamma-glutamyl transferase of 113 which could be attributed to chronic alcohol intake. Ultrasound abdomen and pelvis showed a prominent portal vein measuring 12.9 mm showing hepatopetal fetal flow with pressure support ventilation of 22.4 cm/s and mild splenomegaly.

Autoimmune workup revealed ANA 2+ with mixed nuclear granular and cytoplasmic granular patterns (Fig. 2). ANA profile showed 3+ for RNP, Sm, dsDNA, and 2+ for nucleosomes and histones. C3 level 63.60 mg/dL (low level). Coagulation work-up revealed elevated activated partial thromboplastin time (APTT) of 51.3s and International Normalized Ratio (INR) of 0.91. Lupus anticoagulant and cardiolipin immunoglobulin G (IgG) were also positive. The renal function test showed serum creatinine of 0.84 and 24 h urine protein was 1136. Renal biopsy was done in view of proteinuria which revealed focal proliferation with membranous glomerulonephritis. Score/grade: International Society of Nephrology/Renal Pathology Society classification class III (A)+V. Activity score is 6/24 and disability impairment factor showed diffuse and global granular deposits along glomerular capillary loops and in the mesangium with antisera to IgG (3+), immunoglobulin A (IgA) (2+), immunoglobulin M (IgM) (2+), C3c (2+), Kappa (3+), Lambda (3+) and C1q (2+).

Skin biopsy from the rashes did not show any features of vasculitis and direct immunofluorescence for IgG, IgM, IgA and C3 were negative.

He was given four doses of 250 mg of IV methyl prednisolone once daily for 4 days. In view of secondary APLA, he was started on 2 mg nicoumalone (acitrom). Then, the patient was discharged with oral prednisolone 30 mg OD, Mycophenolate mofetile 360 mg BD and hydroxychloroquin 200 mg BD.

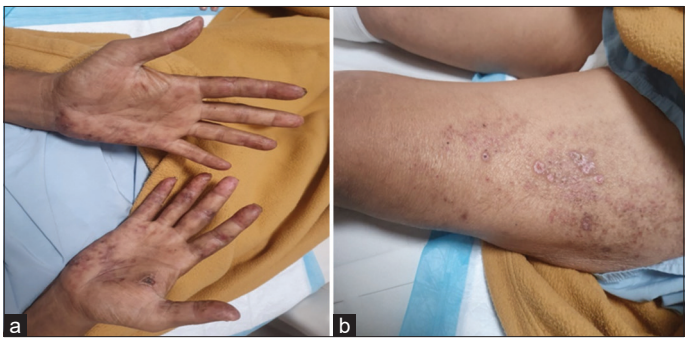

Figure 1: Maculopapular rash over the (a) palm and the (b) left thigh

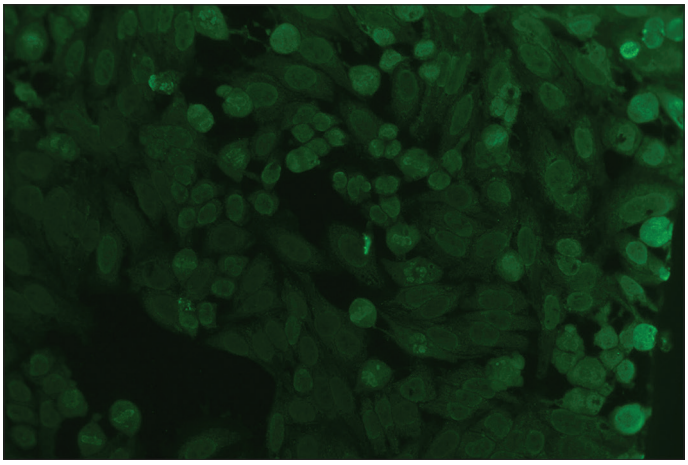

Figure 2: Antinuclear antibody immunofluorescence showing mixed nuclear granular and cytoplasmic granular pattern

DISCUSSION

Systemic lupus erythematosus is a chronic multi-organ disease, symptoms differ in each individual, and can be intermittent depending on the organ system involved and the severity of the disease [6]. It involves the cutaneous manifestation of typical rashes or vasculitic rashes, musculoskeletal involvement of polyarthritis, and myopathy, neurological manifestation of cognitive disorder, acute confusional state, aseptic meningitis, and hematological manifestations of hemolytic anemia, thrombocytopenia, leukopenia, splenomegaly, and lymphadenopathy [7].

Renal manifestations in SLE can be varied and can involve any compartment – glomeruli, tubulointerstitium, and vessels. Most common among them is lupus nephritis which affects 50–60% of patients in the initial 10 years of illness [8]. Recognizing lupus nephritis in SLE is of utmost importance as the goal of management varies depending on the class of nephritis. Hence, renal biopsy is mandatory in patients of SLE with features of nephritis, proteinuria, or hematuria.

Antiphospholipid syndrome (APLA) occurs in 30–40% of patients with SLE, but only 10% of those patients have clinical features of APLA [9]. A prolonged APTT level with positive anti-cardiolipin antibodies or detection of lupus anticoagulant with dilute Russell viper venom time is diagnostic of APLA in SLE [10].

Treatment guideline depends on the severity of the disease. In case of life-threatening, initial management involves a high dose of glucocorticoids with additional second line agents of cyclophosphamide, mycophenolate mofetil, or

calcineurin inhibitors [11]. In non-life threatening illnesses, low-dose glucocorticoids followed by conservative treatment with nonsteroidal anti-inflammatory drugs, antimalarials (hydroxychloroquine, chloroquine, and quinacrine), and biologics such as belimumab (anti-BAFF) and anifrolumab (anti-IFN type 1 receptor) [12].

This patient had a non-life threatening illness with class III lupus nephritis, hence he was managed with low-dose glucocorticoid with second-line agent. The guideline does not recommend immunosuppressive for class I, II, and VI lupus nephritis, whereas, class II, IV, and V require cytotoxic or immunosuppressive agents.

Lupus and APLA, warfarin, or Vitamin K antagonists are preferred, whereas, direct oral anticoagulants are not effective [13]. A target INR of 2.0–2.5 is recommended for patients with one episode of venous clotting; an INR of 3.0–3.5 is recommended for patients with recurring clots or arterial clotting, particularly in the central nervous system.

Our case highlights the importance of importance of renal biopsy and lupus anticoagulant in a patient with SLE. High degree of suspicion should be kept for lupus nephritis is the most common association with SLE and as class VI lupus nephritis are irreversible organ damage.

CONCLUSION

SLE is protean in its manifestations and follows a relapsing and remitting course. Disease severity is wide-ranging. SLE can present major challenges because of accrued organ damage and coagulation defects. Early identification and treatment of associated conditions holds a good prognosis in SLE. Poor prognosis (~50% mortality in 10 years) in most series is associated with (at the time of diagnosis) high serum creatinine levels (>1.4 mg/dL), hypertension, nephrotic syndrome (24-h urine protein excretion >2.6 g), anemia (hemoglobin <12.4 g/dL), hypoalbuminemia, hypocomplementemia, antiphospholipid antibodies, male sex, ethnicity (African American, Hispanic with mestizo heritage), and low socioeconomic status. Hence, adequate clinical suspicion and testing for associated diseases in SLE when necessary are crucial in determining long-term prognosis in lupus patients.

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